

EDITORIAL



Maintenance and resuscitation fluids for brain injury: keep them salty and not too sweet but mind the kidney

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Although intravenous fluids are a fundamental part of routine care for patients with acute brain injury, their selection has been driven by long-standing assumptions, rather than conclusive evidence [1]. It is generally assumed that hypoosmolar solutions cause fluid shifts into the brain, contributing to secondary brain injury. However, evidence regarding the optimal types of intravenous fluids for both resuscitation (i.e., correction of hypovolemia and shock) and maintenance (i.e., meeting water and electrolyte requirements) in patients with acute brain injuries remains limited. Here, we aim to critically assess available guidelines and recent evidence on types of IV fluids, asking ourselves the question: when an ICU patient with acute brain injury requires IV fluids for resuscitation or maintenance, which component should be administered, and to which patients?

Resuscitation fluids—better salty than sorry: when chloride is the safer choice

Resuscitation fluids in critical care have been extensively studied in recent years, with a substantial body of data available to inform long-standing debates. One such discussion focuses on the comparison between NaCl 0.9% and balanced solutions that replace chloride with alkalinizing agents such as lactate in Hartmann's solution and acetate and gluconate in Plasmalyte 148 (electronic supplementary Table 1). It took many studies, culminating in meta-analyses of over 30,000 patients, to show that in critically ill patients balanced solutions have a high

likelihood (90%) of slightly reducing mortality (by 0.4%) compared to NaCl 0.9% [2]. However, traumatic brain injury (TBI) appears to represent an exception: several large clinical trials and subsequent secondary analyses demonstrated that Plasmalyte was associated with higher 90-day mortality in TBI patients [3, 4]. The most probable explanation for this association is that Plasmalyte is slightly hypo-osmolal (theoretical osmolality 295 mOsm/kg, where the actual osmolality is rather 271 mOsm/kg) [5]. Therefore, the use of balanced solutions for the resuscitation of brain-injured patients should be avoided, as was clearly stated in recent guideline and consensus report recommendations, as well as recent systematic reviews (summarized in Table 1).

Can we safely recommend NaCl 0.9% in neurocritical populations, then? Although we remain cautious in interpreting the typical associations between hyperchloremia and mortality—given the clear correlation between chloride levels, administered volume, and the severity of the underlying condition—there is no compelling reason to assume that the predominantly renal consequences of hyperchloremia do not apply to these patients [6, 7]. A dedicated post hoc analysis of the COBI trial was almost certainly underpowered to detect this effect [8]. While the brain may tolerate chloride better than hypo-osmolality, the kidneys may not. To solve this conundrum, reducing chloride burden by using balanced hypertonic solutions, enriched with either acetate or lactate, has been explored in pilot trials, showing the potential to reduce chloride load without losing the therapeutic effect of hyperosmolar solutions [9–11]. Furthermore, in brain-injured patients, augmented renal clearance is more common and may theoretically counteract part of the direct renal arterial vasoconstrictive effect of hyperchloremia

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Table 1 Most recent guidelines and consensus statements for choice of fluids in patients with traumatic brain injury (TBI), aneurysmal subarachnoid hemorrhage (aSAH), and intracerebral hemorrhage (ICH) and updates based on systematic reviews

Comparison or type of fluid (→) Study/publication	Type of evidence: -Guideline or consensus recommendation (G/C) -Systematic review or meta-analysis (SR) -Subgroup analysis of RCTs (sRCT)	Normal (or hypertonic) saline vs. Balanced fluids -Resuscitation (r) -Maintenance (m)	Albumin* -Resuscitation (r) -Maintenance (m)	Glucose-containing fluids -Resuscitation (r) -Maintenance (m)	Comment
2018 Fluid consensus ^b	C	> > We suggest using crystalloids as first-line resuscitation fluids in NIC patients with low blood pressure (Weak recommendation) (r) > > We recommend the use of crystalloids as preferred maintenance fluids in NIC patients (Strong recommendation) (m) > > We suggest against the use of hypertonic saline solutions as resuscitation fluids in NIC patients with low blood pressure (Weak recommendation) (r) > > We suggest monitoring electrolytes (Na⁺, Cl⁻) as a safety endpoint for fluid therapy in NIC patients (Weak recommendation)	> > We recommend against the use of [.] albumin as maintenance fluid in NIC patients (Strong recommendation) (m) > > We recommend against the use of low-dose (4%) albumin as resuscitation fluid in NIC patients with low blood pressure (Strong recommendation) (r) > > We suggest against the use of high-dose (20–25%) albumin as resuscitation fluid in NIC patients with low blood pressure (Weak recommendation) (r)	> > We recommend against the use of glucose-containing hypotonic solutions [.] as resuscitation fluid in NIC patients with low blood pressure (Strong recommendation) (r) > > We recommend against the use of [.] glucose-containing hypotonic solutions [.] as maintenance fluid in NIC patients (Strong recommendation) (m)	In these consensus guidelines, the distinction between different types of crystalloids (normal saline and balanced crystalloids) was not (yet) made for the final recommendations
2019 SIBICC consensus ^c	C	No recommendations	No recommendations	No recommendations	–
2022 AHA/ASA guidelines ICH ^d	G	No recommendations	No recommendations	No recommendations	–
2023 AHA/ASA SAH guidelines ^e	G	No recommendations	No recommendations	No recommendations	Although fluid management and early goal directed therapy were much more strongly emphasized in these guidelines compared with the 2012 guidelines, there is no specific guidance on types of fluids
2023 NCS SAH guidelines ^f	G	No recommendations	No recommendations	No recommendations	–
2024 ACS best practice guideline TBI ^g	G/C	No recommendations	No recommendations	No recommendations	–
2024 ICM guideline choice of resuscitation fluids ^h	G	> > We suggest using isotonic saline rather than balanced crystalloids for volume expansion in adult critically ill patients with TBI (Conditional recommendation, very low certainty of evidence) (r + m) Remark: "More hypotonic balanced crystalloids, such as Ringer's lactate (or acetate), probably should be avoided in patients with TBI"	> > We suggest using isotonic saline rather than albumin for volume expansion in adult critically ill patients with TBI (Conditional recommendation, very low certainty of evidence)	No recommendations	–

Table 1 (continued)

Comparison or type of fluid (→) Study/publication	Type of evidence: -Guideline or consensus recommendation (G/C) -Systematic review or meta-analysis (SR) -Subgroup analysis of RCTs (sRCT)	Normal (or hypertonic) saline vs. Balanced fluids -Resuscitation (r) -Maintenance (m)	Albumin ^a -Resuscitation (r) -Maintenance (m)	Glucose-containing fluids -Resuscitation (r) -Maintenance (m)	Comment
BEST-living systematic review and meta-analysis (2024) ⁱ	SR/sRCT Systematic review and patient-level meta-analysis of 6 RCTs comparing balanced crystalloids vs. normal saline	Normal saline vs. balanced crystalloids (Ringer's lactate or plasmalyte A or 148)	–	–	High likelihood of lower in-hospital mortality in traumatic brain injury with saline
Diz et al. Systematic review and meta-analysis (2025) ^j	SR/sRCT Systematic review assessing effect of balanced crystalloids vs. normal saline in 15 clinical trials	–	–	–	Lower mortality in TBI vs. non-TBI critically ill patients with normal saline vs. balanced crystalloids
Clinical implications		Normal saline is the preferred fluid for TBI to decrease mortality For other types of acute brain injury (SAH, ICH) evidence is insufficient to prefer normal saline over balanced solutions	Albumin solutions are not preferred for resuscitation nor maintenance in brain-injured patients due to lack of evidence and some evidence of harm (especially in case of hypoosmolar albumin fluids)	Glucose-containing hypoosmolar fluids are not advised for resuscitation nor maintenance Most evidence comes from subgroup analyses from large trials in critically ill patients	There is a dearth of clinical trials primarily aimed at TBI and other types of brain injuries comparing the use of different types of fluids Most evidence comes from subgroup analyses from large trials in critically ill patients

ACS American College of Surgeons, TBI traumatic brain injury, SAH subarachnoid hemorrhage, AHA/ASA American Heart/Stroke Association, ICH intracerebral hemorrhage, ICM Intensive Care Medicine (journal)

^a Other colloids than albumin were not included here given the lack of new studies on (synthetic) colloids as fluids for resuscitation or maintenance fluid therapy and the fact that they were not advised in the 2018 fluid therapy consensus

^b Oddo et al. (2018) Fluid therapy in neurointensive care patients: ESCM consensus and clinical practice recommendations. Intensive Care Med 44:449–463

^c Hawryluk et al. (2019) A management algorithm for patients with intracranial pressure monitoring: the Seattle International Severe Traumatic Brain Injury Consensus Conference (SIBICC). Intensive Care Med 45:1783–1794

^d Greenberg et al. (2022) 2022 Guideline for the management of patients with spontaneous intracerebral hemorrhage; a guideline from the American Heart Association/American Stroke Association. Stroke 53:e282–e361

^e Hoh et al. (2023) 2023 Guideline for the management of patients with aneurysmal subarachnoid hemorrhage: a guideline from the American Heart Association/American Stroke Association. Stroke 54:e314–e370

^f Treggiari et al. (2023) Guidelines for the neurocritical care management of aneurysmal subarachnoid hemorrhage. Neurocrit Care 39:1–18

^g <https://www.facs.org/media/vgfgjrkf/best-practices-guidelines-traumatic-brain-injury.pdf>

^h Arabi et al. (2024) European Society of Intensive Care Medicine clinical practice guideline on fluid therapy in adult critically ill patients. Part 1: the choice of resuscitation fluids. Intensive Care Med 50:813–831

ⁱ Zamperli et al. (2024) Balanced crystalloids versus saline for critically ill patients (BEST-Living): a systematic review and individual patient data meta-analysis. Lancet Resp Med 12:237–246

^j Diz et al. (2025) Effect of treatment with balanced crystalloids versus normal saline on the mortality of critically ill patients with and without traumatic brain injury: a systematic review and meta-analysis. Anesth Analg 141:152–161

contributing to acute kidney injury (electronic supplementary Fig. 1). Iso-oncotic albumin 4% has been plagued with a bad reputation since the well-known SAFE trial, where its use (in a hypotonic core solution) was associated with increased mortality in a subgroup of patients with traumatic brain injury and guidelines have aligned with this evidence (Table 1). However, whether albumin dissolved in an isotonic solution is harmful or beneficial in brain injury warrants further study [12].

Maintenance fluids—tonicity versus glucose: what really drives the risk?

Maintenance fluids are prescribed essentially for patients who lack alternative sources of water and electrolytes and are typically used when there are difficulties in administering nutrition. Outside neurocritical care, these fluids are hypotonic to mirror normal water and sodium intake and provide some caloric support to prevent starvation ketosis. However, their use becomes problematic in TBI, where hypotonic fluids may exacerbate cerebral edema. The primary question centers on whether glucose dissolved in an isotonic solution, such as NaCl 0.9%, remains detrimental to brain-injured patients, or if its caloric support might offer potential benefits. Temporal variations in glucose metabolism following TBI and the challenging-to-quantify degree of blood–brain barrier disruption complicate the development of clear recommendations [13]. Regardless, recent evidence emphasizes the critical importance of tightly regulating glycemic levels and preventing both hypo- and relative hyperglycemia in patients with acute brain injury, indicating a lower tolerance compared with other ICU patients for even moderate glycemia up to 11.9 mmol/L [14]. Pending further evidence, it may be prudent to carefully assess the necessity of maintenance fluids, particularly given that multiple sources of water and electrolytes are co-administered in the ICU, including the volumes used to dissolve medications. As such, *fluid creep* refers to the unintended accumulation of fluids administered for medications or fluid challenges in the absence of clear hypovolemia or low preload, as confirmed by advanced hemodynamic monitoring, potentially leading to unnoticed fluid overload. In the multicenter randomized COBI trial of 370 patients with moderate to severe traumatic brain injury, continuous infusion of 20% hypertonic saline as a maintenance fluid for at least 48 h did not significantly improve 6-month neurological outcomes compared to standard care alone [15]. Although the intervention was safe and associated with a slight, non-significant reduction in intracranial hypertension and mortality, the wide confidence intervals suggest the study may have been underpowered to detect meaningful clinical effect.

Conclusion

Current best practices regarding types of fluids in brain injury patients are largely based on pathophysiological reasoning and subgroup analyses from larger randomized trials. Patient with acute brain injuries, especially those with TBI, appear to represent a different subgroup regarding preferred IV fluids among all critically ill. Given the limited available evidence, we recommend that future research investigate the following: the relationship between hyperchloremia, augmented renal clearance, and acute kidney injury (AKI); the effects of balanced versus non-balanced hypertonic solutions on renal and neurological outcomes; the role of albumin or glucose in non-hypotonic solutions; and how different types of brain injuries may impact the benefits versus side effects of (un)balanced crystalloids.

Supplementary Information

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Declarations

Conflicts of interest

NvR is a co-founder of the International Fluid Academy (fluidacademy.org), which is supported by unrestricted educational grants from the industry. He has also received speaker and advisory board fees from Baxter Healthcare. MvdJ reports no conflict of interest in relation to this topic.

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